REMARKS

I. Introduction

Claims 34-39 and 41-64 are pending in the application. Of the above claims, 39, 41-43 and 51-64 are withdrawn from consideration. Claims 34-38 and 44-50 are under consideration.

II. Rejection under 35 U.S.C. §102

The Examiner maintains his rejection based on US 2003/0235820 (hereinafter "Mack et al.").

As a preliminary matter, Applicant notes that the Examiner responds to comparisons of TKT-L1 expression in PrimC to NormC. However, the claims do not explicitly recite such a comparison involving NormC. To facilitate prosecution and clarify the claims, Applicant has amended claim 34 to recite "detecting in . . . a normal control test sample a level of expression of a transketolase like-1 . . . . " Support for this amendment may be found throughout the specification as filed and specifically on page 3, lines 8-14, of the application as filed.

The Examiner bases his argument on a theory that Mack et al., like claim 1, teaches that "diagnosis of a disorder characterized by abnormal cell proliferation is indicated when the level of expression in the biological test sample is greater than said level of expression in the normal control test sample . . . " (Office Action p. 5). Applicant respectfully submits that Mack et al. fails to teach a NormC level of expression in a control sample, as recited in claim 1. The Examiner specifies that "[e]xamples with non-metastatic tissue as 'normal' tissue are taught in Table 17 [of Mack et al.], which includes TKTL-1 expression" (Office Action, page 6). Applicant refers to Table 17 of Mack et al, which is entitled "B survivor vs Mets –Up in B survivor." Mack et al. explains in paragraph [0041] that "[i]n Tables 1-26, the ratio provided represents **primary tumor samples *from* known Dukes B stage survivors** vs. liver metastasis samples from patients with metastatic colorectal cancer." In other words, Table 17 shows PrimC > MetC, and makes no mention of NormC. Applicant respectfully believes that the Examiner may be misreading the title of Table 17 and interpreting samples from cancer survivors to be normal tissue rather than tissue **from tumors** taken from the survivors.

Hence, Mack et al. fails to teach a method of detecting a disorder characterized by abnormal cell proliferation when the level of expression of TKTL1 in a test sample is higher than a level of expression of TKTL1 in anormal control sample. Mack et al. makes

comparisons of PrimC to MetC, but fails to teach a comparison of levels of expression of transketolase like-1 in PrimC v. NormC. Therefore, Mack et al does not teach the method of detecting disorders of abnormal cell proliferation utilizing a normal level of expression as does claim 34.

In view of the foregoing remarks, Applicant respectfully requests that the Examiner withdraw the rejection under 35 U.S.C. §102.

III. Rejections under 35 U.S.C. §112 Second Paragraph

Under 35 U.S.C. §112, the Examiner makes several rejections due to the claims being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

First, beginning at the bottom of page 8 of the Office Action, the Examiner rejects claim 34 for failing to mention whether a presence or an absence of a disorder of abnormal proliferation is indicated when the level of expression in the test sample is "greater than" the control sample. Applicant respectfully believes that the previously presented language of "a diagnosis of at least one of said disorders" would be interpreted by one of skill in the art to mean "a diagnoses of *a presence of* at least one of said disorders". However, in order to facilitate prosecution, Applicant has amended the claim 34 largely in accordance with the language suggested by the Examiner in the paragraph bridging pages 13-14 of the Office Action, although not including the limitations suggested by the Examiner directed to colon cancer.

Second, the Examiner rejects claim 49 for a minor issue involving lack of antecedent basis. Applicant has amended claim 49 to address this matter.

Third, the Examiner rejects claim 50 for presenting "an in vitro or in vivo method" while depending on claim 34 which involves only "An in vitro method". Applicant has amended claim 50 to recite only "an in vitro method."

IV. Rejections under 35 U.S.C. §112 First Paragraph

A. Possession of the Invention

The Examiner presents several rejections under 35 U.S.C. §112 for failing to comply with the written description requirement.

First, the Examiner rejects the language reciting "a sequence having at least 80% homology to SEQ ID NO: 1" and asserts that the specification only provides support for "a transketolase like-1 gene whose complement hybridizes under stringent conditions to . . . SEQ ID NO: 1." In order to facilitate prosecution, Applicant amends claims 34 and 44 to remove the references to 80% homology.

Second, beginning at the bottom of page 13 of the Office Action, the Examiner rejects claims 34-38 and 44-50 due to the broad claim language of diagnosing "at least one of said disorders characterized by abnormal cell proliferation" rather than diagnosing only "colon cancer". The Examiner asserts that only methods of detecting colon cancer are enabled by the specification. However, Applicant respectfully asserts that not only does the specification support the diagnosis of cancers other than colon cancer, but also evidence exists in the art that methods of detecting colon cancer could be used to detect other disorders characterized by abnormal cell proliferation.

Specifically, in the originally filed specification, TKTL1 was described as having been found overexpressed in colorectal cancer (p. 39 lines 8-10), colon carcinoma (p. 37 lines 27-28), lung adenocarcinomas (p. 37, lines 27-28), and carcinomas of the stomach (p. 37, lines 27-29). Further, the specification as filed explicitly states that staining for TKTL1 could be observed in breast-, lung-, cervical-, gastric-, oesophageal-, endometrial-, and ovarian-carcinomas (p. 39 lines 4-7).

Outside evidence that methods of detecting colon cancer could be applied to other types of cancer includes the enclosed documents Exhibit 1- Exhibit 11. The enclosed document Exhibit 1, (Langbein et al., British Journal of Cancer (2006) 94, 578-584), discloses that the overexpression of TKTL1 also occurs in bladder-, breast-, thyroid-, prostate-, pancreas-, ovarian-, cervix-, rectal-, and kidney carcinomas as well as in melanoma and glioblastoma (*see esp.* page 580. right column, second paragraph). The cancers mentioned in Exhibit 1 belong to the most aggressive cancer types of all. Exhibit 1 as well as the enclosed documents Exhibit 2 (Földi et al.), Exhibit 6 (Staiger et al.), Exhibit 7 (Völker et al.), Exhibit 8 (Langbein et al.), Exhibit 9 (Völker et al.), Exhibit 10 (Kayser et al.) and Exhibit 11 (Krockenberger et al) demonstrate for several different types of tissues that in cases of overexpression of TKTL1 in abnormal proliferating cells an aggressive tumor is present, forming or capable of forming metastasis and potentially resulting in the death of the respective individual.

Applicant respectfully submits that the documents Exhibit 3 (test protocols of the Applicant), Exhibit 4 (Zhang et al.) and Exhibit 5 (Xu et al.) demonstrate that tumors of various cancers degenerate after application of TKTL1 inhibitors. The aforementioned papers describe experiments with TKTL1 as target molecule for anti-cancer-drugs and in combination reveal that an inhibition of TKTL1 indeed results in an inhibition of tumor cell proliferation. From these papers it is apparent that skilled persons in the art followed the statements of Coy, disclosed in the current application that the overexpression of TKTL1 indicates the presence of cancer, and that the inhibition of TKTL1 might be a way of treating cancer. Zhang et al. and Xu et al. carried out appropriate experiments that confirm the statements of Coy.

For instance, Exhibit 5 Xu et al. recites in the abstract, "The anti-transketolase-like-1 small interfering RNA construct significantly decreased the level of transketolase in the transfected human colon cancer cell line cells, arrested them in G0/G1 phase and substantially inhibited cell proliferation." Xu et al. further recites in the abstract, "Our data demonstrated that the transketolase-like-1 gene plays an important role in total transketolase activity and in the cell proliferation of human colon cancer.'

Furthermore, Exhibit 4 Zhang et al. discloses in the abstract an association of TKTL1 with cancer of the liver in HepG2 cells:

> We inhibited the expression of TKTL1 by RNAi in HepG2 cells. It was found that total transketolase activity was dramatically downregulated and the proliferation of cancer cells was significantly inhibited in HepG2 cells. These results indicate that TKTL1 gene influences total transketolase activity and cell proliferation in human hepatoma cells, suggesting that TKTL1 gene plays an important role on glycometabolism in tumors and it might become a novel target for tumor gene therapy.

All of the experiments set forth in the enclosed exhibits could not be incorporated in the original specification of the patent application because their performance would have required too much time and would have postponed the filing date of the present application for an unacceptably long period of time. However, the Exhibits prove that others of skill in

the art followed the teaching of the claim 34 that TKTL1 overexpression is indicative of the presence of disorders characterized by abnormal cell proliferation, including but not limited to colon cancer. Furthermore, the works of others as well as experimental data of the inventor confirm the accuracy of claim 34.

B. New Matter

In the final section beginning on page 18, the Examiner rejects the claims for presenting new matter. Particularly, the Examiner asserts that the specification does not support methods of detecting complements of genes that hybridize under stringent condition to a sequence having at least 80% homology to SEQ ID NO: 1. To facilitate prosecution, Applicant deletes the phrase "a sequence having at least 80% homology".

In view of the above remarks, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. §112.

V. CONCLUSION

In view of the foregoing, reconsideration and withdrawal of all rejections and allowance of the application is respectfully solicited.

If the Examiner believes that a telephone conversation with the Applicant's attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned, Blair R. Lanier, at the telephone number shown below.

The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for any retroactive extensions of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,

AKERMAN SENTERFITT

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